REMARKS

Applicants have amended claims 43 to 47 to limit the claims to a method of reducing immune-mediated damage associated with graft versus host disease. Claims 48-56, 58 and 59 have been cancelled. Claims 57 has been amend to makes its limitations consistent with those of claims 43-47. Claim 60 has been added to specify administration to bone marrow transplant patients. No new matter has been added by these amendments.

Rejections Under 35 U.S.C. §112, first paragraph

The Examiner rejected claims 43-50 and 52-59 as allegedly not enabled. The Examiner stated that the claims were enabled only for immune-mediated damage caused by CIK cells. Claims 48-56, 58 and 59 have been cancelled. The pending claims are limited to a "method for reducing immune-mediated damage to cells, tissues or organs associated with graft versus host disease" This limitation was present in previously pending claim 49.

Applicants disagree with the Examiner's conclusion that the claimed methods are enabled only for treatment of immune mediated damage caused by CIK cells. The specification describes studies demonstrating that a fusion polypeptide consisting of Hsp47 (SEQ ID NO:6) fused to Gst protected mice receiving a bone marrow transplant from the symptoms of graft versus host disease. As explained on page 55 of the specification, all five irradiated control mice that received bone marrow and spleen derived cells from a mice of a different strain along with Gst protein host exhibited the classic symptoms of graft versus host disease—fur ruffling and weight loss. Significantly, four of the five mice died over the four week observation period. In contrast, none of the five irradiated experimental mice receiving bone marrow cells and spleen derived cells from mice of a different strain along with Hsp47-Gst fusion protein exhibited the symptoms of graft versus host disease. Importantly, none of these mice died over the four week observation period. These studies demonstrate the ability of Hsp47 to protect against immune mediated damage associated with graft versus host disease. Moreover, this murine bone marrow transplant model is one which is accepted by those in the art as highly useful for modeling host versus graft disease. Thus, these studies alone demonstrate that the present specification enables

one skilled in the art to make and to use the presently claimed invention for reducing immune-mediated damage associated with host versus graft disease.

The Examiner previously argued that the claims were enabled only for the reduction of immune-mediated damage caused by CIK cells. It should be noted that the murine bone marrow transplant studies described above did not involve the administration of CIK cells. Thus, it is clear that, contrary to the Examiner's assertions, the enablement provided by the present specification is not limited damage caused by CIK cells.

Despite the clear demonstration in the specification that Hsp47 can reduce host versus graft disease, the Examiner never individually addressed the enablement of previously pending claim 49, which was limited to "immune-mediated damage is caused by graft-versus-host disease". Applicants recognize that the present Office Action is a Final Office Action. However, Applicants respectfully request that the Examiner fully consider the present claims as they include only limitations that were in previously pending claims, yet were not addressed by the Examiner.

The present specification also demonstrates that fragments of Hs47 are immunoprotective. For example, the specification also describes studies demonstrating that Hsp47 as well as a fragment thereof having the amino acid sequence AVLSAEQLR (SEQ ID NO:3) selectively protects endothelial cells (HUVEC cells) from killing by CIK cells while not significantly inhibiting the lysis of tumor cells by CIK cells. This study demonstrates that a Hsp47 fragment having the amino acid sequence AVLSAEQLR (SEQ ID NO:3) can provide protection against immune-mediated damage. This study demonstrates that an active fragment of Hsp47 containing AVLSAEQLR (SEQ ID NO:3) can be immunoprotective. The presently claimed methods are drawn to the use of such peptides

The present claims are limited to "methods reducing immune-mediated damage to cells, tissues or organs associated with graft versus host disease" by administering an immunoprotective amount of a composition comprising a polypeptide that includes AVLSAEQLR (SEQ ID NO:3). In view of the forgoing, it is Applicant's position, that the pending claims meet the enablement standard of 35 U.S.C. §112, first paragraph, and Applicants respectfully request that this rejection be withdrawn.